World Bipolar Day
5th Annual Research Symposium

PROGRAM

CAMH Centre for Youth Bipolar Disorder
March 26th, 2026 | Toronto, Canada

TEMERTY FACULTY OF MEDICINE
UNIVERSITY OF TORONTO

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WELCOME MESSAGE

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Dear Colleagues and Friends,

Welcome to the Centre for Youth Bipolar Disorder's 5th annual World Bipolar Day Research Symposium. We have a great programme featuring fabulous keynote speakers, additional leading Canadian researchers, and early career investigators. This is the second year that members of our Youth Advisory Council are participating in a variety of roles. The theme of this year's symposium is "*Energizing Bipolar Disorder Research: Integrating Brain, Biology, and Behavior*." Energy imbalance, and particularly energy deficits, are a leading driver of functional impairment and reduced quality of life among people living with bipolar disorder. In parallel, mitochondrial dysfunction is consider a core mechanism underlying bipolar disorder. Our keynote speakers each view the energy-mitochondria-bipolar nexus through a different lens, and we are looking forward to the insights that will emerge from their convergent perspectives.

Many thanks to those who have travelled internationally and from across Canada to join us in person, and to local attendees whose presence here helps advance our goal of increased collaboration and networking. This symposium brings together Canadian and International researchers, trainees, clinicians and mental health professionals to take part in presentations and discussions on current research and clinical knowledge in bipolar disorder, with a special emphasis on youth bipolar disorder and connections between physical and mental health.

Established in 2009, and based at the Centre for Addiction and Mental Health since 2020, CYBD is among the largest and most productive groups focused on youth bipolar disorder worldwide. Our primary research themes relate to the heart-brain-mind interface, suicide risk reduction, and concurrent disorders. We also conduct related clinical trials, including dialectical behavior therapy, exercise, and novel pharmacologic approaches. Our mission is to improve outcomes for youth with bipolar disorder through cutting-edge research, treatment, education, and advocacy. We seek to generate discoveries uniquely relevant to youth with bipolar disorder, an illness that remains vastly under-studied even in comparison with other psychiatric disorders.

We hope that this year's symposium is educational, thought provoking, and inspiring. We wish to extend our heartfelt gratitude to the youth with lived experience of bipolar disorder who are actively involved in this year's symposium. We are both proud and honored to partner with you.

Hoping that you find the day informative, inspiring, thought-provoking, and engaging. Please throw your weight into the culture of this day, by meeting new people, exchanging ideas, and sharing something of what you learn today with people in your circles. Thank you for joining us!

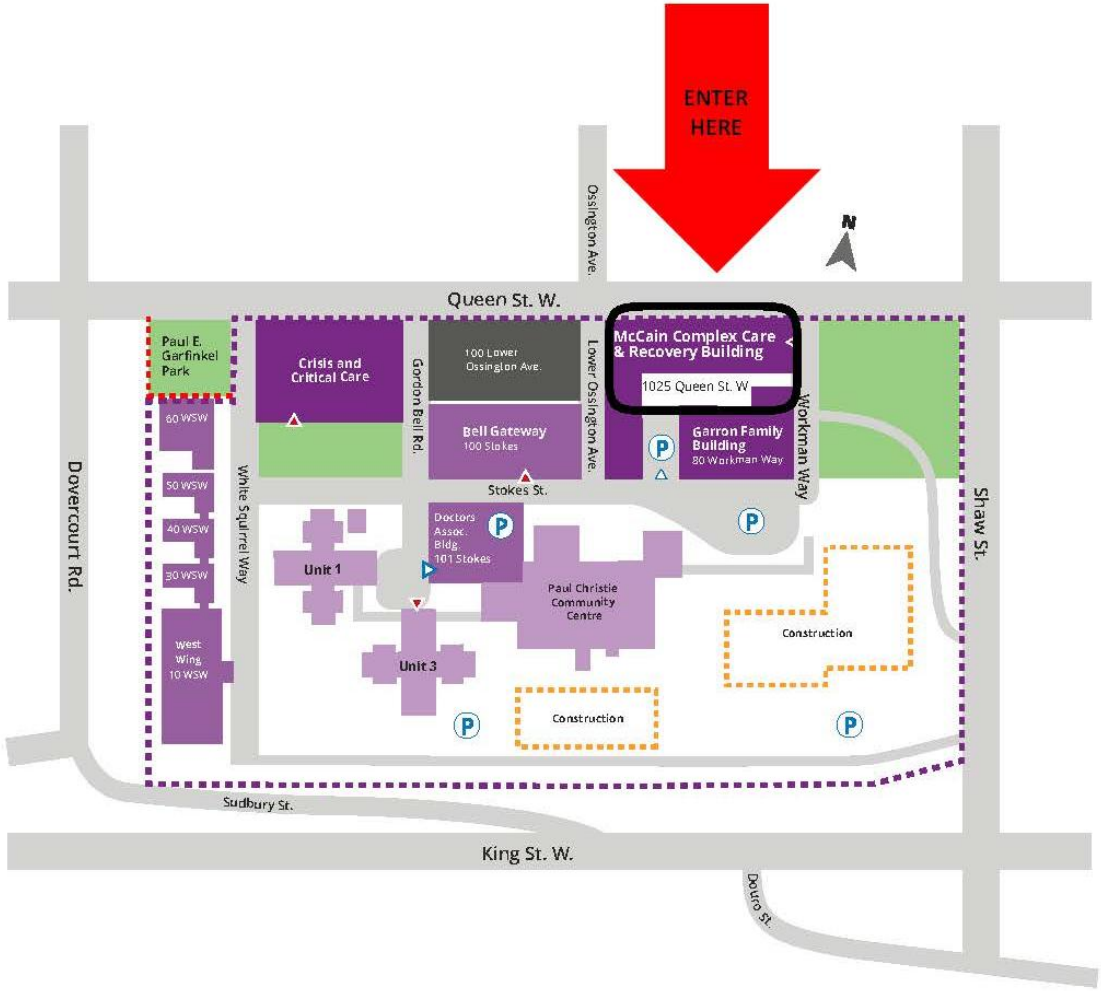
Warm regards,

Benjamin I. Goldstein, MD, PhD, FRCPC

PROGRAMME AT A GLANCE

Wi-Fi network: CAMHGuest

Wi-Fi password: Welcome2CAMH



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CYBD World Bipolar Day

McCain Complex Care & Recovery Building

1025 Queen Street West

2nd floor Auditorium

***Please use the North entrance on Queen Street West**

CYBD staff will be there to greet you!

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PROGRAMME AT A GLANCE

8:30-9:00 AM	**REGISTRATION**
9:00-9:15 AM	**WELCOME AND OPENING COMMENTS** **Dr. Benjamin Goldstein,** Director of CYBD **Noah** and **Sunny**, CYBD Youth Advisors
9:15-10:00 AM	**KEYNOTE LECTURE 1** **Dr. Louisa Sylvia, PhD,** Associate Professor, Harvard Medical School *"Exercise as a Treatment for Bipolar Disorder"*
10:00-10:50 AM	**KEYNOTE LECTURE 2** **Dr. Ana Andreazza, PhD,** Professor, Department of Pharmacology & Toxicology, University of Toronto: *"Bioenergetic, Neuronal, and Calcium Signaling Phenotypes in Bipolar Disorder"*
10:50-11:05 AM	**COFFEE BREAK**
11:05-11:50 AM	**KEYNOTE LECTURE 3** **Dr. Alessandro Colasanti, MD, PhD,** Associate Professor in Biological Psychiatry, Brighton and Sussex Medical School: *"Mitochondrial vulnerability, respiratory dynamics and regulation of subjective energy: Imaging Neurometabolism to Understand and Target Mood Instability in Bipolar Disorder"*
11:50 AM -12:30 PM	**POSTER PRESENTATIONS**
12:30-1:45 PM	**NETWORKING LUNCH**
1:45-2:50 PM	**RAPID PRESENTATIONS** ***Novel Treatment Targets and Innovation in Mood Disorders*** **Chair: Kristen Li** **Dr. Jess Fiedorowicz, MD, PhD** Head and Chief of Mental Health, Professor, Department of Psychiatry, The Ottawa Hospital *"BD² Integrated Network"* **Dr. Elisa Brietzke, MD, PhD,** Professor, Department of Psychiatry, Queen's University *"What should we know about nutrition and Bipolar Disorders: Findings from the NExT ISBD Task Force"* **Dr. Rodrigo Mansur, MD, PhD,** Assistant Professor, Department of Psychiatry, University of Toronto *"Semaglutide for the Treatment of Major Depressive Disorder: A Randomized Clinical Trial"*

PROGRAMME AT A GLANCE

2:50-3:10 PM	**AFTERNOON COFFEE BREAK**
3:10-4:15 PM	**RAPID PRESENTATIONS** ***Predicting Risk and Understanding Mechanisms in Bipolar Disorder*** **Chair: Sunny** **Dr. Tomas Hajek, MD, PhD,** Professor, Faculty of Medicine, Department of Psychiatry, Dalhousie University *"Low BMI as a risk factor for future weight gain related hippocampal atrophy"* **Dr. Aroldo Dargél, MD, PhD,** Associate Professor, Faculty of Medicine, Department of Psychiatry, University of Ottawa *"One-Year Hospitalization Risk in Youth Bipolar Disorder: A Multimodal AI Approach Using EMR Data"* **Julius März, PhD Student,** Erasmus Medical Center Rotterdam: *"Examining daily affect intensity and variability in adolescent offspring of parents with depressive or bipolar disorder"*
4:15-4:30 PM	**CLOSING REMARKS AND THANK YOU** Dr. Benjamin Goldstein, Director of CYBD

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Live educational activities, occurring in Canada, recognized by the Royal College of Physicians and Surgeons of Canada as Accredited Group Learning Activities (Section 1) are deemed by the European Union of Medical Specialists (UEMS) eligible for ECMEC®.

Dr. Louisa Sylvia, PhD | 9:15 AM

Associate Director, Dauten Family Center for Bipolar Treatment Innovation, Massachusetts General Hospital
Associate Professor of Psychology, Department of Psychiatry, Harvard Medical School

Exercise as a Treatment for Bipolar Disorder

Introduction: Bipolar disorder (BD) is often characterized as an energy disorder given that its defining feature is severe and unpredictable shifts in energy levels, not just mood. These energy shifts have been tied to mitochondrial dysfunction because it disrupts energy production leading to oxidative stress within brain cells, creating a biphasic energy pattern where energy is abnormally high in mania and low in depression. Exercise may help by increasing mitochondrial turnover, improving brain energy production, reducing inflammation, and enhancing neuroplasticity.

Methods: We will review exercise interventions for BD, including a pilot study of a lifestyle intervention that we developed for BD, or the Nutrition Exercise and Wellness Treatment (NEW Tx). In this study, participants were randomized to NEW Tx (n = 19) or a treatment as usual waitlist (n = 19).

Results: A recent meta-analysis of 7 RCTs (n=576) demonstrated that exercise significantly improves depressive symptoms and anxiety symptoms in BD (p's <.05), but not manic symptoms. Similar results were observed in NEW Tx, such that increased exercise was associated with decreased depressive symptoms and improved functioning (p's <.05). Subgroup analyses in the meta-analysis found that duration ≤1 hour/session, frequency >5 sessions/week, and intervention period ≤12 weeks produced more pronounced improvements in depressive symptoms.

Conclusion: These data suggest that exercise is a feasible intervention for BD which can improve outcomes. We will discuss potential mechanisms and aspects of exercise interventions that are important to maximize outcomes.

Disclosures: *Dr. Sylvia has received grant funding from PCORI, NIH, HRSA, Tiny Blue Dot Foundation, and AFSP. She has also received funding as a member of the Miliken Institute's Scientific Advisory Board as well as royalties form New Harbinger for her two, published books on bipolar disorder.*

Dr. Ana Andreazza, PhD | 10:00 AM

Professor, Department of Pharmacology and Toxicology, University of Toronto

Bioenergetic, Neuronal, and Calcium Signaling Phenotypes in Bipolar Disorder

Background: Psychiatric disorders frequently accompany primary mitochondrial diseases (PMDs), implicating mitochondrial dysfunction as a shared biological substrate for psychiatric vulnerability. To determine how familial mitochondrial risk influences neuronal development in bipolar disorder (BD), we generated induced pluripotent stem cells (iPSCs), neural progenitor cells (NPCs), and cortical neurons (CNs) from three healthy controls (CT), three patients with BD, and three patients with BD and a family history of mitochondrial disease (BD-FMD).

Methods: Across differentiation, we assessed mitochondrial function (ATP production, mitochondrial membrane potential, ROS generation, cytosolic cell-free mtDNA), metabolomic signatures, calcium imaging, and neuronal electrophysiological activity through multi-electrode arrays (MEA).

Results: BD neurons exhibited pronounced hyperexcitability, whereas BD-FMD neurons displayed prolonged mitochondrial calcium transients, altered membrane potential, and aberrant ROS, consistent with a sustained energetic deficit. Metabolomic profiling revealed distinct pathway enrichments in BD and BD-FMD, indicating divergent bioenergetic adaptations to mitochondrial burden.

Conclusions: Our findings reveal that familial mitochondrial liability actively reshapes neuronal differentiation and function, producing distinct trajectories of mitochondrial performance, calcium signaling, and network excitability. These results suggest that mitochondrial dysfunction in BD is not a secondary byproduct of illness, but a mechanistic contributor to altered neuronal energetics and communication. Together, these findings delineate how inherited mitochondrial vulnerability reshapes neuronal excitability and metabolism, revealing bioenergetic phenotypes that may inform precision stratification and therapeutic targeting in BD.

Disclosures: *No commercial disclosures.*

Dr. Alessandro Colasanti, MD, PhD | 11:05 AM

Associate Professor, Department of Clinical Neuroscience, Brighton and Sussex Medical School, University of Sussex

Mitochondrial vulnerability, respiratory dynamics and regulation of subjective energy: Imaging neurometabolism to understand and target mood instability in bipolar disorder

Neurometabolic instability—rooted in mitochondrial dysfunction, disrupted oxidative capacity, and dynamic shifts in cerebral respiration and metabolic fluxes—may provide a unifying biological mechanism for the episodic energy surges, neuroprogression and mood instability that is characteristic of bipolar disorder. In this lecture, I will integrate converging evidence from quantitative neuroimaging, pharmacological metabolic challenges, and controlled respiratory paradigms to illustrate how transient disturbances in neurometabolism can reshape neuronal function and affective regulation. I will present human studies demonstrating abnormal oxidative neurometabolic responses to methylene blue in BD, alongside findings in individuals with primary mitochondrial disorders showing elevated anterior cingulate lactate associated with daily fluctuations in subjective energy. Building on a newly developed functional MRS (fMRS) paradigm, the lecture will illustrate how dynamic changes in lactate production and cerebrovascular responses can be captured during sustained emotional and cognitive engagement, offering real-time insight into the energetic state of key mood-regulating circuits. By integrating neurometabolic imaging biomarkers with clinical observations and lived-experience narratives, we can begin to characterise the specific physiological transitions that occur during hypomanic or depressive states. Although still in its nascent, early conceptual stage, this emerging framework has the potential to transform care by guiding the development of patient-centred treatments that act on core brain-energy regulatory processes—from targeted mitochondrial interventions to personalised behavioural and respiratory strategies—ultimately paving the way for precision approaches that target mood regulation, and possibly attenuate, or prevent mood-episode onset.

***Disclosures**: No commercial disclosures.*

O.1 BD² Integrated Network

Presenting Author: Dr. Jess Fiedorowicz, MD, PhD; *Head and Chief of Mental Health, Professor, Department of Psychiatry, The Ottawa Hospital, Ottawa, Ontario, Canada*

Recognizing an urgent need to drive progress in bipolar disorder research and care, BD² has developed an Integrated Network to bring together an unprecedented depth of information from people with bipolar disorder to effectively lift the ceiling on current scientific understanding, create new treatment options, and drive a path towards wellness. The BD² Integrative Network currently involves 11 sites in the US and Canda. The presentation will be given by the Lead PI of the inaugural Canadian site in Ottawa, Ontario. The network sites participate in a longitudinal cohort study and a learning health network. The BD² Integrated Network works to improve the health and well-being of people living with bipolar disorder by engaging a network of collaborating investigators and clinicians to implement and inform data-driven improvements in care, build an unprecedented data ecosystem comprised of longitudinal clinical and biological data, and generate novel insights that will drive innovative approaches to bipolar disorder interventions and treatments. The presentation will provide an overview of the BD² Integrative Network and the data being collected in advance of an upcoming public data release of comprehensive, pre-processed, cross-site baseline data from 615 Integrated Network participants.

Disclosures: None.

O.2 Semaglutide for the treatment of major depressive disorder: A randomized clinical trial

Presenting author: Dr. Rodrigo B. Mansur, MD, PhD; *Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada*

Background: There has been increasing interest and speculation on the potential neuropsychiatric effects of glucagon-like peptide 1 receptor agonists (GLP-1RAs). To our knowledge, no study has evaluated the efficacy and safety of a GLP-1RA for the treatment of major depressive disorder (MDD) in a randomized clinical trial.

Methods: This was a 16-week, randomized, double-blind, placebo-controlled, parallel-group trial. Eligible adults met DSM-5–defined criteria for MDD, exhibited pre-treatment evidence of cognitive impairment and were overweight/obese. Patients were randomized (1:1) to receive placebo or oral semaglutide 14 mg, adjunctive to their treatment as usual. The primary efficacy outcome was an executive function composite score. Secondary outcomes included a global cognition composite score, as well as measures of functioning, depressive symptom severity, reward behavior and suicidality.

Results: 72 participants were randomized to oral semaglutide (n = 35) or to placebo (n = 37). In the primary analysis, oral semaglutide did not improve executive function. Preplanned secondary analysis showed treatment effects for global cognition and effort-based decision-making. Adjunctive semaglutide also improved health-related quality of life through metabolic and motivational pathways, independent of mood symptoms. There was no effect of treatment on depressive symptom severity, nor on suicidal ideation. Gastrointestinal side effects were common on semaglutide, although there were no serious adverse events.

Conclusion: Semaglutide did not significantly improve executive function; results from secondary analyses suggested effects on specific domains of cognition and reward. Semaglutide was safe for patients with MDD. These findings support the potential of metabolic interventions to advance recovery-oriented outcomes in depression.

Disclosures: This work was supported by a grant from the Physicians' Services Incorporated Foundation.

O.3 Low BMI as a risk factor for future weight gain related hippocampal atrophy

Presenting Author: Dr. Tomas Hajek, MD, PhD; *Department of Psychiatry, Dalhousie University, Halifax, Nova Scotia, Canada*

Introduction: Individuals with Bipolar Disorder (BD) are at an increased risk of becoming overweight/obese, and frequently display smaller hippocampal volumes. It is unclear how weight/weight gain and BD interact in their longitudinal effects on the brain.

Methods: In collaboration with the ENIGMA-BD Working Group, we obtained T1-weighted MRI scans from 944 participants, including 233 with BD, scanned in 13 international sites at two time points on average 2.84±1.63 years apart. We used linear mixed models to assess the bidirectional relationship between baseline BMI or BMI change and hippocampal volume or volume change, adjusting for age, sex, and ICV and modelling interactions with BD. While the hippocampus was our a priori region of interest we repeated these analyses in other subcortical regions.

Results: Baseline BMI predicted future hippocampal atrophy, but baseline brain structure did not predict future weight changes. BMI increased significantly over time in both groups (F (1,1085) = 15.98, p < 0.001). Individuals with lower baseline BMI experienced greater weight gain (F(1,922) = 105.12, p < 0.001). Greater weight gain was associated with greater hippocampal atrophy over time (F(1,899) = 16.33, p = 0.001), more so in BD than CN (F(1,898) = 6.91, p = 0.009). Consequently, lower baseline BMI predicted greater future hippocampal volume loss (F(1,904) = 14.77, p < 0.001). These associations were not replicated in other subcortical regions.

Conclusions: Our findings suggest that weight gain is a modifiable risk factor for hippocampal atrophy, especially in individuals with low to normal BMI and those with BD. Prevention of weight gain, especially in people with BD, could provide neuroprotective benefits.

Disclosures: None.

O.4 One-Year Hospitalization Risk in Youth Bipolar Disorder: A Multimodal AI Approach Using EMR Data

Presenting Author: Dr. Aroldo A. Dargél, MD, PhD; *University of Ottawa, Ottawa, Ontario, Canada*

Background: Patients with bipolar disorder (BD) are at heightened risk of psychiatric hospitalization, yet the drivers of adverse illness trajectories—especially within the first year after diagnosis—remain unclear. Emerging applications of artificial intelligence (AI), including machine learning (ML) applied to electronic medical records (EMR), offer improved predictive accuracy and interpretability. This study aimed to predict psychiatric hospitalization within 365 days of an initial BD diagnosis in youth aged 18 to 30.

Methods: A total of 1,024 youths aged 18 to 30 with a new BD diagnosis were identified from EMR at The Ottawa Hospital (Ontario, Canada) between 2019 and 2024. The mean age was 24.15 (SD = 3.34), and 57.2% were female. Clinical and sociodemographic features used to develop four ML prediction models. Model performance was assessed using standard metrics, and interpretability was examined using SHAP to quantify feature contributions.

Results: The strongest-performing model achieved 80% accuracy in predicting psychiatric hospitalization at 1-year follow-up. Across four models, the most influential predictors were manic symptoms, suicidal ideation, bizarre behavior, and cannabis use. Treatment with lithium or antipsychotics at the time of BD diagnosis were associated with reduced predicted risk of hospitalization.

Conclusion: Models predicted 1-year psychiatric hospitalization with up to 80% accuracy. Manic symptoms, suicidal ideation, and cannabis use were the most influential predictors of higher hospitalization risk, while lithium and antipsychotic treatment at diagnosis were associated with lower predicted risk. Interpretable AI approaches may support personalized risk stratification by quantifying

individual risk and clarifying which factors drive predictions.

Disclosures: None.

O.5 Examining daily affect intensity and variability in adolescent offspring of parents with depressive or bipolar disorder

Presenting Author: Julius März, MSc; *Department of Child and Adolescent Psychiatry/Psychology, Erasmus Medical Center, Rotterdam, Netherlands*

Introduction: Adolescent offspring of parents with mood disorders, like depression or bipolar disorder, show increased risk for developing mood disorders themselves. However, little is known about their daily emotional experiences compared to adolescents with healthy parents. To address this, we examined affect intensity (i.e. average positive and negative affect over two weeks) and affect variability (i.e. RMSSD per participant in positive and negative affect) in high-risk adolescents (parents with mood disorders) and controls (parents without mood disorders), and related these daily affect dynamics to internalizing and externalizing mood disorder symptoms.

Methods: In this preregistered study, we used data from the Mood and Resilience in Offspring (MARIO) project, one of the largest studies worldwide on risk and resilience in high-risk offspring. 352 participants, aged 10–25 years, reported internalizing and externalizing symptoms through the YSR and ASR and completed a two-week ecological momentary assessment (EMA), measuring affect five times daily. Participants had parents with mood disorders (bipolar, depressive, psychotic, or postpartum disorder) or no mood disorders (control group).

Results: High-risk offspring (n = 249) did not differ significantly from controls (n = 103) in positive or negative affect intensity or variability. However, adolescents with higher internalizing symptoms exhibited lower positive affect intensity, higher negative intensity, and greater negative affect variability, but similar positive affect variability compared to those with fewer symptoms.

Conclusions: Daily affective experiences may not differ based on familial risk. Rather, daily affect dynamics are associated with concurrent mood disorder symptoms regardless of whether their parents are affected by depression or bipolar disorder.

Disclosures: None.

P.1 Brain structural improvements following bariatric surgery: A coordinate-based meta-analysis

Presenting Authors: Julia Fraiha-Pegado, MSc;
Dalhousie University, Halifax, Nova Scotia, Canada

Introduction: Obesity is increasingly linked to reduced grey matter (GM) volume, white matter integrity, and functional connectivity, specifically within the hippocampus. While bariatric surgery is a highly effective intervention for significant weight loss and reducing mortality, its specific neuroanatomical impacts remain poorly synthesized. This study aimed to appraise available literature and quantify the extent of brain changes following surgical weight loss interventions.

Methods: We conducted a systematic search using PubMed and Scopus to identify longitudinal MRI studies investigating brain structure changes after bariatric surgery. We used Seed-based d Mapping (SDM-PSI) to conduct a coordinate-based meta-analysis. Resulting GM volume changes were then visualized using MRIcronGL. Study quality was assessed using the Newcastle-Ottawa Scale (NOS).

Results: Five studies met inclusion criteria (n = 161, mean age = 27.6 – 51.1 years). Following surgical interventions individuals lost on average, between 8.5 to 11 BMI points. Meta-analysis results showed significant GM increases in the right cerebellum at an average follow-up of 8.4 months (SDM-Z = 2.59, p = 0.019) even after family-wise error correction. At an uncorrected level, additional improvements were observed in right lenticular nucleus/putamen, right fusiform gyrus, BA48, left cerebellum and right lingual gyrus.

Conclusions: Our findings suggest that significant weight reduction following bariatric surgery is linked to overall improvement in several brain regions, most pronounced in the right cerebellum. Our findings indicate that surgical weight loss may reverse some obesity related neuroanatomical declines. Future research should focus on incorporating longer follow-up periods as well as cognitive assessments to determine if these structure changes translate into functional improvements.

Disclosures: None.

P.2 The influence of obesity and hippocampal atrophy on cortical structure in bipolar disorders - An ENIGMA study in 934 participants

Presenting Author: Dr. Sean McWhinney, MSc, PhD;
Dalhousie University, Halifax, Nova Scotia, Canada

Introduction: This study investigated the relationship between BMI changes, hippocampal volume, and cortical thickness over time in bipolar disorder, building on previous research linking obesity and hippocampal atrophy.

Methods: Data were collected through the ENIGMA BD working group, including cortical thickness and subcortical volume derived using FreeSurfer from structural MRI data, and BMI. Participants had two MRI scans, on average 2.84 years apart. We used linear mixed regression modeling to test for associations between BMI, hippocampal volume, and cortical thickness of 34 regions, controlling for possible confounds and reporting FDR-adjusted p-values.

Results: Among 233 patients and 701 healthy controls, during an average of 2.84 years between scans, weight gain was associated with hippocampal atrophy ($t(904) = -3.39$, $p = 0.001$). Moreover, hippocampal atrophy was associated with cortical thinning in 32 of 34 regions. However, BMI increase was only associated with cortical thinning in four of these regions.

Conclusion: Weight-gain related loss of hippocampal volume was associated with reduction in cortical thickness over time in most cortical regions. At the same time, only a small proportion of cortical regions also showed association with weight gain. The change in hippocampal volume seems to be associated with cortical thickness changes, which are mostly uncoupled from the initial insult. This could be an example of brain plasticity secondary to a relatively focal change. Future research should investigate the processes/mechanisms involved in such propagation of tissue loss throughout the brain.

Disclosures: None.

P.3 A Bridge to Better Days: A pilot study of a multimodal intervention to support the successful transition from hospital to community care for people living with bipolar disorder

Presenting Author: Daniela Giansante, HBSc; *McMaster University, St. Josephs Healthcare, Hamilton, Ontario, Canada*

Introduction: Individuals with recent-onset bipolar disorder (BD) often experience poor illness insight, leading to reduced treatment adherence and an increased risk of relapse. Insight-related challenges are especially pronounced in young adults, as BD typically emerges in late adolescence or early adulthood. The first year following hospitalization is a uniquely vulnerable period for young adults with recent-onset BD, with relapse rates reaching up to 57% as they must independently manage community reintegration, self-care, and medication routines with limited support.

Objectives: This pilot study aims to evaluate the feasibility, acceptability, and preliminary effectiveness of a 6-month multimodal intervention designed to improve illness insight and support the transition from hospital to community care in recent-onset BD.

Methods: Ten young adults (ages 18-35) diagnosed within the past 24 months and recently discharged from hospital-based care will receive: (1) six group psychoeducation sessions; (2) twelve 1:1 peer-support sessions; and (3) two individualized educational sessions for their primary healthcare providers. Feasibility will be assessed through recruitment and retention rates, and acceptability through patient-reported satisfaction scores and stakeholder feedback. Illness insight will be measured pre- and post-intervention using the Mood Disorder Insight Scale (MDIS). Descriptive statistics will summarize feasibility and acceptability, and paired-samples t- tests will examine changes in insight and clinical outcomes.

Results: With high recruitment and retention (≥80%), the intervention may demonstrate directional improvements in illness insight, supporting adherence after discharge.

Conclusion: Findings will inform a larger randomized controlled trial and may help shape future standards of BD care for individuals early in their diagnosis.

Disclosures: None.

P.4 Loneliness in Adolescents and Youth with Bipolar Disorder

Presenting Author: Tanya Tanya, MSc; *The Ottawa Hospital, Ontario Canada*

Introduction: Bipolar disorder (BD) typically emerges in adolescence, when mood instability and interpersonal difficulties increase vulnerability to poor outcomes. Loneliness—a transdiagnostic construct linked to psychiatric illness and physiological dysregulation—is especially prevalent during this developmental stage. This review synthesizes evidence on loneliness in adolescents and youth with BD.

Methods: We systematically searched PubMed, PsycINFO, Embase, and CINAHL from inception to July 2025 using the terms “bipolar,” “loneliness,” and “adolescents/youth.” Peer-reviewed studies were eligible without language or date restrictions if they included participants with a formal diagnosis of BD and examined loneliness/ social isolation. The review followed the PCC framework, JBI Reviewer’s Manual, and PRISMA-ScR guidelines.

Results: The six studies included 522 adolescents and young adults with BD. Across methodologies, loneliness and social isolation consistently emerged as key features—predicting diagnostic status, linking to altered neural responses to social exclusion, and often preceding mood episodes. Social isolation was common but largely maladaptive, and data identified it as a significant psychosocial risk factor.

Conclusion: This review is the first to synthesize evidence on loneliness in adolescents and young adults with BD. Longitudinal and mechanistic studies are needed to clarify its interplay with mood,

cognition, and biological stress systems. Clinically, routine assessment and targeted interventions may help reduce its impact and improve outcomes for this vulnerable population.

Disclosures: None.

P.5 Clozapine use in treatment resistant mood disorders – A chart review

Presenting Author: Julia Zabielska; *McMaster University, Hamilton, Ontario, Canada*

Aim: We aim to investigate the long-term clinical course of patients with treatment-resistant mood disorders who are taking clozapine.

Methods: We identified all patients with a diagnosis of mood disorder, either bipolar disorder (BD), major depressive disorder (MDD) or schizoaffective disorder (SZA) being treated with clozapine at the St. Joseph's Healthcare Hamilton's Mood Disorders Treatment and Research Clinic. After a comprehensive chart review, we extracted clinical and demographic data over the course of their clozapine treatment, such as number of hospitalizations and suicide attempts.

Results: Twenty-five patients currently treated with clozapine were identified (BD=17, MDD=6, SZA =2) with a mean chart review timeline length of 17.52 years (SD = 5.77). The mean age of patients as of 2025 was 58.68 (SD=11.08). Paired-sample t-test were conducted on patients with sufficient chart information to compare the number of hospitalizations while the patient was not taking clozapine (M=4.63, SD=4.78), and taking clozapine (M=1, SD=2.15). Patients had significantly less hospitalizations (t=-3.34, p=0.004, n=19) while on clozapine. Patients also had significantly less suicide attempts while on clozapine (M=0.087, S=0.29) if compared to before starting the medication (M=1.30, S=2.03) (t=-2.92, p=0.008, n=23).

Conclusion: Our study provides additional support to the potential benefits of long-term clozapine use in the clinical course of patients with treatment-resistant mood disorders. The results of this study may encourage clinicians to use clozapine for this challenging population of treatment-resistant mood disorder patients with high hospitalizations and suicidal attempts.

Disclosures: Dr. Gomes has received honoraria (consultant and speaker) from Abbvie, Lundbeck and Otsuka outside of this work. All other authors have no commercial disclosures.

P.6 N-acetylaspartate and obesity: A meta-analysis

Presenting Author: Cameron MacGillivray; *Department of Psychiatry, Dalhousie University, Halifax, Nova Scotia, Canada*

Introduction: Obesity is highly prevalent in bipolar disorder (BD) and has been increasingly associated with alterations in brain structure, yet the neurobiological mechanisms underlying these changes remain poorly understood. Proton magnetic resonance spectroscopy (^{1}H-MRS) provides a mechanistic approach by quantifying neurometabolites such as N-acetylaspartate (NAA), a suggested marker of neuronal integrity. Although emerging evidence suggests that obesity may be associated with altered neurometabolite profiles, findings remain limited and methodologically heterogeneous.

Methods: To clarify whether obesity, measured by body mass index (BMI), is reliably associated with altered brain NAA levels, an effect-size meta-analysis of adult ^{1}H-MRS studies was conducted. A systematic search of PubMed, Embase, and Scopus identified studies reporting neural NAA concentrations and BMI. Due to variability in reporting practices, two analytic approaches were employed: categorical comparisons between healthy-weight and overweight (BMI ≥ 25) and continuous analyses examining the full BMI range.

Results: Across eligible studies, higher BMI was associated with lower NAA in frontal regions in both models (categorical: d = -0.49, 95% CI [-0.95, -0.03], p = .03, k = 6; continuous: r = -0.24, 95% CI [-0.35, -0.12], p < .001, k = 6). An additional categorical difference was observed in the right hippocampus (d

= -0.52, 95% CI [-0.85, -0.19], p = .002, k = 4), though based on fewer studies.

Conclusions: Overall, these findings provide preliminary evidence that higher BMI is associated with reduced NAA, particularly in frontal regions, further motivating standardized region-specific MRS research, especially in high-risk populations, such as those with BD.

Disclosures: None.

P.7 The clinical profile of forensic inpatients with bipolar disorder at a Canadian high-security institution

Presenting Author: Dane Mauer Vakil; *University of Waterloo, Ontario, Canada*

Introduction: The prevalence of violent criminality is higher among individuals with bipolar disorder (BD) compared to the general population, with comorbid substance use playing a key role. In Ontario, an estimated 7% of forensic hospital inpatients have BD, and over half are also diagnosed with a substance use disorder. However, no research has examined the clinical presentation of this population. This study provides a clinical profile of forensic inpatients with BD at a Canadian secure forensic program.

Methods: A retrospective analysis was conducted using clinical data from Waypoint Centre for Mental Health Care. The sample consists of 61 male forensic inpatients with BD. Variables of interest include offense severity, institutional violence, psychotic behaviours, mood disturbances, history of alcohol and drug addiction, and adverse childhood experiences.

Results: 41% of the sample committed a violent offense resulting in hospitalization, with 98% of the sample having had a psychiatric admission prior to the incident. Drug and alcohol use prior to age 18 was common, with 35% having consumed alcohol before/during the offense. The prevalence of psychotic behaviours, mood disturbances, and inappropriate or procriminal behaviours varied across the sample.

Conclusion: This study establishes baseline knowledge regarding the criminal history, institutional behaviour, and clinical presentation of forensic inpatients with BD. These findings are essential for improving clinical practice and informing policy development in Canada. By providing health system decision makers with key insights into this population, this research will support evidence-informed policy decisions regarding the organization and delivery of forensic hospital services.

Disclosures: None.

P.8 Considering mental disorders in cardiovascular disease prediction models: A cross-sectional survey of primary care providers

Presenting Author: Sara Siddiqi; *University of Ottawa, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada*

Introduction: Cardiovascular disease (CVD) prediction models are used in primary care settings to determine the likelihood of a patient developing heart disease. These risk calculators include CVD risk factors, yet they rarely incorporate mental disorders, which can lead to two-fold increases in risk. The perspectives of primary care providers on accessibility and barriers of model use remains a key gap in risk calculator development. We aim to: 1) Determine primary care provider perspectives on the clinical accessibility of mental disorder-related information, 2) Identify barriers of risk calculator usage.

Methods: A cross-sectional web-based survey hosted on SurveyMonkey was developed in consultation with experts, and pilot tested by a committee of primary care providers. The survey link was distributed to all departments of family medicine in Canada (n=17), and faculties of nursing at the same institutions, for sharing in their networks. In addition, existing contacts/residency groups were requested to share the survey. Eligible participants were family physicians, family medicine residents, and nurse practitioners in Canada. A Likert scale was used to rate the accessibility of variables, and open-ended

questions were used to collect feedback on prediction model usage.

Results: To date there have been 120+ eligible responses, >70% are female, 80% practice in community clinics, >50% are family physicians, and prediction models are reportedly used an average of 82% of the time for patients at risk of CVD. Survey recruitment is currently on-going; results will be finalized prior to presentation.

Conclusions: Identifying clinically accessible variables will inform future CVD risk calculator development.

Disclosures: None.

P.9 Clocks in Sync: A pilot trial of combined chronotherapies for mania in bipolar disorder

Presenting Author: Jess G. Fiedorowicz; *University of Ottawa, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada*

Introduction: Bipolar disorder (BD) is often accompanied by disruptions in sleep and circadian rhythms. Yet, chronotherapies, which target circadian rhythms, are seldom used in practice. From our engagements, persons with lived and living experience (PWLEs) find these treatments to be of great interest, especially blue-blocking glasses (BBG) and time-restricted eating (TRE). The combination of these two treatments is of particular interest given that TRE targets peripheral clocks and BBG target a central clock.

Methods: We conducted a randomized, three group parallel pilot trial to assess the feasibility of TRE (10:14 of diurnal eating to nocturnal fasting based on PWLE input) as an adjunctive treatment for mania in an inpatient setting. Patients were randomized 1:1:1 to TRE, BBG or both. Feasibility was assessed through monitoring of adherence and qualitative semi-structured interviews with participants and staff to identify any challenges/barriers to implementation, and what supports might be needed. The data analyst and raters were blinded to outcomes.

Results: Twenty-one participants consented for the trial. 76% of participants were mostly adherent or better with no differences in adherence across groups. Themes from qualitative data highlighted key challenges in adhering to treatment. The secondary outcome of efficacy based on the Young Mania Rating Scale is currently blinded but will also be presented.

Conclusions: Circadian interventions requiring active participation can reasonably be administered in high acuity, inpatient settings with most able to adhere to interventions. Our pilot study may inform future studies or clinical implementation of these and other low cost and scalable circadian interventions.

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P.10 Real-Time Assessment of the Dynamics Between Cognitive Effort and Glucose Metabolism in Healthy and Clinical Populations

Presenting Author: Ryan M. Brudner; *Poal Hansen Centre for Depression, University Health Network, Toronto, ON, Canada; Institute of Medical Science, University of Toronto, Toronto, ON, Canada*

Introduction: Anhedonia, a core symptom of major depressive disorder (MDD), manifests as reduced motivation and effort expenditure for rewards. Anhedonia and reward dysfunction have been linked to dysregulated glucose metabolism. While lab-based tasks like the Effort Expenditure for Rewards Task (EEfRT) reveal motivational deficits in MDD, real-time dynamics in daily life remain underexplored. Continuous glucose monitoring (CGM) and ecological momentary assessment (EMA) offer ecologically valid tools to examine these associations.

Purpose and Hypothesis: This pilot study assesses the feasibility of integrating CGM, actigraphy, and EMA-based assessment of reward behavior to investigate real-time relationships between glucose levels and cognitive effort in MDD and healthy controls (HC). We hypothesize that higher blood

glucose will be associated with increased willingness to expend effort for rewards, but this association will be attenuated in MDD participants.

Methods: Thirty-two adults (16 MDD, 16 HC; aged 18-65, BMI/sex-matched) will undergo screening, baseline assessments (mood, cognition, metabolic), and 14 days of daily-life monitoring: blinded CGM (FreeStyle Libre Pro iQ), actigraphy (ActiGraph), and EMA via Expiwell app (4 prompts/day; effort/reward choices: low-effort/low-reward vs. high-effort/high-reward, $0.50-$4.50). Feasibility metrics include adherence rates, device functionality, and data quality. Exploratory analyses use generalized estimating equations and computational modeling (subjective value models) to examine glucose-effort associations.

Results and Conclusion: Preliminary data (n=11; 7 MDD, 4 HC) show 83% EMA adherence and 91% CGM/actigraphy data validity. Recruitment is on track. Initial behavioral patterns indicate variability in effort choices, with MDD trending toward fewer hard-task selections. This protocol demonstrates feasibility for real-time motivational phenotyping in MDD, paving the way for larger studies targeting glucose-metabolism interventions.

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P.11 Development and Structural Validity of a Brief Version of the Life Problems Inventory, a measure of Borderline Personality Disorder symptoms in youth

Presenting Author: Kiefer Cowie; *Centre for Addiction and Mental Health, Toronto, Ontario, Canada*

Introduction: The Life Problems Inventory (LPI) is a 60-item self-report measure developed to assess symptoms of borderline personality disorder in young people. The underlying factor structure of the LPI has not been evaluated as it was originally developed based on a theoretical framework rather than including factor analytic methods. We sought to evaluate the structural validity of the LPI and to create a briefer version for use with youth.

Methods: Data was collected from youth (N=704; M age=16; range=13-20) with or at risk for bipolar disorder, and controls, seen at a research centre focused on youth with bipolar disorder. Factor analysis indicated questionable structural validity of the original LPI and thus we developed a brief version from the ground up. We divided the sample into training and testing subsamples. The training stage consisted of using exploratory and confirmatory factor analysis along with professional and lived experience expertise to develop a 20-item version of the LPI ("LPI-20"). The LPI-20 was then evaluated in the testing sample using confirmatory methods and measurement invariance testing.

Results: The LPI-20 consists of 5-factors labelled as: "emotion dysregulation", "identity/dissociation", "relationship instability", "self-harm", and "impulsivity". Confirmatory analyses indicated support for this 5-factor model and measurement invariance was achieved across sexes and age groups, but not across clinical and non-clinical groups.

Conclusion: Our findings indicate support for using the total or subscale scores of the LPI-20 with treatment seeking youth. More research is needed to evaluate the generalizability of these findings in addition to establishing scoring benchmarks.

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